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10/645,451	08/21/2003	Joseph L. Bryant	4115-150 CIP DIV	7909

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,451	BRYANT ET AL.	
	Examiner	Art Unit	
	Marcia S. Noble	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *12-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-21 are pending. Claims 1, 2, 5, and 11 are amended by Applicant's response, filed 10/11/2007.

Election/Restrictions

2. Claims 12-21 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/7/2006.

Claims 1-11 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

3. Claims 1-11, as amended and previously presented, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant traverses this rejection on several grounds:

1) The claims lack enablement because a CD4 transgenic rat would not serve as a model of human HIV infection because the binding of CD4 alone does not lead to HIV infection. Applicant argues that the amendment to the claims now recite a model for HIV binding and therefore overcome this point of rejection. Applicant's argument is considered persuasive and therefore, this point of enablement is addressed.

2) The claims lack enablement because the art of producing a transgenic animal with a given phenotype is unpredictable. Applicant argues that specification on pages 22-24 and in example 12 , page 51 provide ample enable to make the instant transgenic rat that serves as a model of human HIV-1 infection.

Applicant's argument has been fully considered and not found persuasive. Pages 22-24 provide general teachings on how to generate a transgenic rat and example 12 prophetically asserts that a double transgenic rat can be made by means provided in example 11. It is acknowledged that methods of producing transgenic rats are described in the specification and known in the art. However, generating a transgenic rat in itself is not the issue of enablement, the issue is generating a transgenic rat with a predictable phenotype (e.i.- results in HIV infection). As previously stated in the Office Action, mailed 7/11/2007 (page 7-8), " Mullins et al teaches that not all animals express a transgene sufficiently to provide a model for a disease as the

integration of a transgene into different species of animal has been reported to give divergent phenotypes (Mullins et al Hypertension 22:631, col 1, par 1, lines 14-17, 1993). The elements of the particular construct used to make transgenic animals are held to be critical, and that they must be designed case by case without general rules to obtain good expression (e.g. specific promoters, presence or absence of introns, etc. (Houdebine J. Biotech 34:281, 1994). Mullins et al disclose that "the use of non-murine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to the another." (Mullins et al. J Clin Invest 98:S39 summary, 1996). Therefore, overall, the art teaches that the production of one species of transgenic animal with a given phenotype does not predictably transfer to the production of transgenic animal of another species." Therefore, because the instant specification only prophetically teaches a transgenic rat with a phenotype of HIV infection and the art teaches that producing phenotypes in a transgenic rat are unpredictable, an artisan would not know how and if production of the transgenic rat taught in the specification would result in a model of human HIV infection. Therefore, this point of enablement is maintained.

3) The claims lack enablement because the art suggests that a double transgenic comprising CD4 and CCR5 or CXCR4 does not represent a model for human HIV-1 infection as taught by Sawada et al and Browning et al. Applicant argues that this art is not applicable because transgenic mouse models are not predictive of

transgenic rat models and transgenic rat models are superior models for human HIV infection because they express gp120 and mouse models do not.

Applicant's arguments are not found persuasive. It is acknowledged that transgenic mouse models are not necessarily predictive of transgenic rat models and that a transgenic rat model *may* serve as a better model of HIV-1 infection because, similar to humans, the rat has gp120 where the mouse does not. However, as previously stated in the Non-Final Rejection, mailed 7/11/2007 on pages 8 and 9, art suggests that additional factors are most likely needed in addition to CD4 elements, CXCR4 or CCR5 for HIV-1 infection that truly mimics HIV-1 infection in humans. As previously stated, "Sawada et al teaches that transgenic mice coexpressing of CD4 and hCXCR4 had significantly lower levels of p24 antigen than that produced by human PBMC following infection with HIV-1 and that this suggests that additional factors are required to efficiently replicate viruses in mouse lymphocytes (p. 1445, col 1). Browning et al state that the coexpression of CD4 and CCR5 in T cells of transgenic mice permitted in vivo HIV-1 infection of the T-cells from these transgenic mice albeit at a much lower level than in human T cells (p. 146410, col 2, par 1). Browning et al further state (p. 14640, col 2, last par) , "Taken together these results suggest that although expression of human CD4 and a chemokine receptor such as CCR5 may be sufficient to permit entry of HIV-1 into mouse cells, the combined effect of impairment in other stated of HIV replication in mouse cell may prevent the development of sustained infection in these human CD4/CCR5 transgenic mice. Therefore, the presence of additional blocks that prevent efficient HIV replication in mouse cells complicates the

use of transgenic mice to investigate the immunopathology of HIV-1 infection." Therefore, the art suggest that are additional factors unique to human HIV-1 infection that are not being accounted for in the art recognized transgenic mice. Therefore, because the art suggests that more factors need to be present in transgenic animal models than CD4 and CCR5 or CXCR4 to model human HIV infection, the sole co-expression of CD4 and CCR5 or CD4 and CCR5 may not provide a sufficient model human HIV infection as claimed. Neither the art nor the specification provides teaching of additional cofactors that may be needed in the making of the CD4/CCR5 transgenic mouse that will model human HIV infection. Therefore, since the art teaches that CD4/CXCR4 or CD4/CCR5 transgenic animals require additional factors to model human HIV infection and neither the art nor the specification teach the factors needed to facilitate a phenotype that would model human HIV, an artisan would not know how to make a CD4/CXCR4 or CD4/CCR5 transgenic rat that models human HIV as claimed."

Furthermore, until the transgenic rat is generated with a means of human HIV-1 infection that is representative of human HIV-1 infection phenotype, it is not clear that these other factors that make human HIV-1 infection unique will or will not play a role in the transgenic rat model. Again, art of Sawada et al and Browning et al further demonstrate the unpredictabilities that may be problematic and are unknown because the instant transgenic rat model has not been reduced to practice or taught in such a manner that overcome the unpredictabilities described in the art. Therefore, again, because the instant transgenic rat is only prophetic and factors that result in humanized HIV-1 infection are unique and unknown, the instant specification does not enable the

instantly claimed transgenic rat models and therefore this point of enablement is maintained.

4) The claims lack enablement because binding requirement for HIV-1 and -2 are different and therefore the instant transgenic rats would not serve as models for HIV in general. Applicant argues that the claims have been modified to recite only HIV-1 and therefore overcome this point of rejection. Applicant's arguments are found persuasive and therefore this point of enablement is addressed.

Therefore, because Applicant's arguments are not fully persuasive and because the issue of unpredictability in enabling a prophetically taught transgenic rat remains, the rejection of record is maintained.

Written Description

4. The rejection of claim(s) 1-11, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn.

The amendments to the claims remove the recitation of a portion of CCR5 and the full CCR5 has adequate written description. The claims still recite a portion of CD4. This recitation is deemed to have adequate written description because between the teachings of the specification and the teaching of the art, a portion of CD4 required for binding has adequate description. Therefore the rejection of record is withdrawn.

New Matter

5. The rejection of claims 1-11 under 35 U.S.C. 112, first paragraph, for reciting the new matter, "wherein the transgenic rat is adapted to model human HIV infection", is withdrawn.

Applicant amended the claims and the claims no longer contain this recitation. Therefore, the rejection is withdrawn.

However, the amendment to the claims necessitates the following new matter rejection.

6. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Amended claim 1 recites, "wherein the transgenic rat is a model for human HIV-1 binding". The specification as originally filed provides no implicit or explicit support for this recitation.

Applicant asserts that page 5, lines 19-23, provide support for this recitation because it discusses non-human transgenic models of disease progression. However, this reference in the specification is to animal models of lentiviral (e.g. HIV) infection and development of disease (e.g. AIDS). It does not teach a model for HIV-1 binding as

claimed. Furthermore, the specification only teaches a model for HIV infection and disease progression. No where in the specification does it teach a model for HIV binding. Therefore, the specification does not provide implicit or explicit support for a model of HIV binding and therefore the recitation constitutes new matter.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. The rejection of claims 1-11, under 35 U.S.C. 112, second paragraph; as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn.

The indefinite recitation, "wherein the transgenic rat is adapted to model HIV infection", has been amended and therefore is no longer recited in the claims. Therefore, the rejection is withdrawn.

Claim 5 recites "capable of mediating entry of HIV". The metes and bounds of this recitation were considered indefinite because the claim did not specify into what HIV is entering. Applicant amended the claims to recite, capable of mediating entry of HIV-1 into the PBMC etc... Therefore, the recitation is no longer indefinite and therefore the rejection is withdrawn.

The amendments to the claims introduce the following 112, second paragraph indefinite issues.

8. Claims 2-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites, "a model of HIV infection" and also recites "a model of HIV binding" because it is dependent on claim 1. Therefore, claim 2 and its dependent claims 3-10 are indefinite because it is not clear if the instant transgenic rat is supposed

to be a model for HIV-1 binding or a model for HIV infection or both a model of binding and infection.

9. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcia S. Noble